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B. Wells
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Amendment And Response Under 37 CFR 1.116
Expedited Prosecution
Art Unit 1655

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellants: Maura C. Cannon, Francis C. Cannon, Gabriel J. McCool, Henry E. Valentin and Kenneth J. Gruys

Serial No.: 09/479,040 Group Art Unit: 1655

Filed: January 07, 2000 Examiner: A. Chakrabarti

For: *POLYHYDROXYALKANOATE BIOSYNTHESIS ASSOCIATED PROTEINS AND CODING REGION IN BACILLUS MEGATERIUM*

Do not Enter
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Anne Kr. Chakrabarti
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Assistant Commissioner for Patents
Washington, D.C. 20231

AMENDMENT AND RESPONSE TO OFFICE ACTION

Sir:

Responsive to the Office Action mailed on October 23, 2001, please amend the claims and consider the following remarks. A Petition for an Extension of Time for one month, up to and including February 23, 2002, and the appropriate fee for a small entity, are enclosed. It is believed that no additional fee is required with this submission. However, should an additional fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-1868.

In the Claims

1. (Twice Amended) An isolated or purified nucleic acid segment comprising a nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein, wherein the nucleic acid sequence

is [selected from the group consisting of:] a nucleic acid sequence at least about 80% identical to SEQ ID NO:8 [which;] that

hybridizes under stringent conditions to SEQ ID NO:8 or the complement thereof;] and

[a nucleic acid sequence encoding] encodes a protein at least about 80% identical to SEQ ID NO:9 [which is immunoreactive with an antibody immunoreactive with SEQ ID NO:9;]

and that has 3-keto-acyl-CoA reductase activity higher for for D-isomers of C6 carbon chains than for C4 carbon chains.

3. (Amended) A recombinant vector comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein;

b) a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein; wherein the structural nucleic acid sequence is [selected from the group consisting of:]

a nucleic acid sequence at least about 80% identical to SEQ ID NO:8; that

[a nucleic acid sequence that] hybridizes under stringent conditions to SEQ ID NO:8 or the complement thereof; and

[a nucleic acid sequence encoding] encodes a protein at least about 80% identical to SEQ ID NO:9[; and

a nucleic acid sequence encoding a protein that is immunoreactive with an antibody prepared using SEQ ID NO:9 as an antigen, the antibody being immunoreactive with SEQ ID NO:9; and] and that has 3-keto-acyl-CoA reductase activity higher for for D-isomers of C6 carbon chains than for C4 carbon chains; and

c) a 3' transcription terminator.

4. (Amended) A recombinant cell comprising a nucleic acid segment encoding a 3-keto-acyl-CoA reductase protein, wherein the nucleic acid segment is [selected from the group consisting of:]

a nucleic acid sequence at least about 80% identical to SEQ ID NO:8; that

[a nucleic acid sequence that] hybridizes under stringent conditions to SEQ ID NO:8 or the complement thereof; and

[a nucleic acid sequence encoding] encodes a protein at least about 80% identical to SEQ ID NO:9[; and

a nucleic acid sequence encoding a protein that is immunoreactive with an antibody prepared using SEQ ID NO:9 as an antigen, the antibody being immunoreactive with SEQ ID NO:9] and that has 3-keto-acyl-CoA reductase activity higher for for D-isomers of C6 carbon chains than for C4 carbon chains.

5. (Amended) A genetically transformed plant cell comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein;

b) a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein; wherein the structural nucleic acid sequence is [selected from the group consisting of:]

a nucleic acid sequence at least about 80% identical to SEQ ID NO:8; that

[a nucleic acid sequence that] hybridizes under stringent conditions to SEQ ID NO:8 or the complement thereof; and

[a nucleic acid sequence encoding] encodes a protein at least about 80% identical to SEQ ID NO:9[; and

a nucleic acid sequence encoding a protein that is immunoreactive with an antibody prepared using SEQ ID NO:9 as an antigen, the antibody being immunoreactive with SEQ ID NO:9;]

and that has 3-keto-acyl-CoA reductase activity higher for for D-isomers of C6 carbon chains than for C4 carbon chains;

c) a 3' transcription terminator; and

d) a 3' polyadenylation signal sequence that directs the addition of polyadenylate nucleotides to the 3' end of RNA transcribed from the structural nucleic acid sequence.

6. (Amended) A genetically transformed plant comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein;

b) a structural nucleic acid sequence encoding a 3-keto-acyl-CoA reductase protein; wherein the structural nucleic acid sequence is [selected from the group consisting of:]

a nucleic acid sequence at least about 80% identical to SEQ ID NO:8[;] that

[a nucleic acid sequence that] hybridizes under stringent conditions to SEQ ID NO:8 or the complement thereof; and

[a nucleic acid sequence encoding] encodes a protein at least about 80% identical to SEQ ID NO:9[; and

a nucleic acid sequence encoding a protein that is immunoreactive with an antibody prepared using SEQ ID NO:9 as an antigen, the antibody being immunoreactive with SEQ ID NO:9;] and that has 3-keto-acyl-CoA reductase activity higher for for D-isomers of C6 carbon chains than for C4 carbon chains;

c) a 3' transcription terminator; and

d) a 3' polyadenylation signal sequence that directs the addition of polyadenylate nucleotides to the 3' end of RNA transcribed from the structural nucleic acid sequence.

9. (Twice Amended) An isolated or purified nucleic acid segment comprising a nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein, wherein the nucleic acid segment is [selected from the group consisting of:]

a nucleic acid sequence at least about 80% identical to SEQ ID NO:10 [which;] that hybridizes under stringent conditions to SEQ ID NO:10 or the complement thereof; and

[a nucleic acid sequence encoding] encodes a protein at least about 80% identical to SEQ ID NO:11 [which is immunoreactive with an antibody immunoreactive with SEQ ID NO:11;] and that has polyhydroxyalkanoate synthase activity.

11. (Amended) A recombinant vector comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein;

b) a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein; wherein the structural nucleic acid sequence is [selected from the group consisting of:]

a nucleic acid sequence at least about 80% identical to SEQ ID NO:10[;] that

[a nucleic acid sequence that] hybridizes under stringent conditions to SEQ ID NO:10 or the complement thereof; and

[a nucleic acid sequence encoding] encodes a protein at least about 80% identical to SEQ ID NO:11[; and

a nucleic acid sequence encoding a protein that is immunoreactive with an antibody prepared using SEQ ID NO:11 as an antigen, the antibody being immunoreactive with SEQ ID NO:11;] and that has polyhydroxyalkanoate synthase activity; and

c) a 3' transcription terminator.

12. (Amended) A recombinant host cell comprising a nucleic acid segment encoding a polyhydroxyalkanoate synthase protein, wherein the nucleic acid segment is [selected from the group consisting of:]

a nucleic acid sequence at least about 80% identical to SEQ ID NO:10[;] that

[a nucleic acid sequence that] hybridizes under stringent conditions to SEQ ID NO:10 or the complement thereof; and

[a nucleic acid sequence encoding] encodes a protein at least about 80% identical to SEQ ID NO:11[; and

a nucleic acid sequence encoding a protein that is immunoreactive with an antibody prepared using SEQ ID NO:11 as an antigen, the antibody being immunoreactive with SEQ ID NO:11] and that has polyhydroxyalkanoate synthase activity.

13. (Amended) A genetically transformed plant cell comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein;

b) a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein; wherein the structural nucleic acid sequence is [selected from the group consisting of:]

a nucleic acid sequence at least about 80% identical to SEQ ID NO:10[;]that

[a nucleic acid sequence that] hybridizes under stringent conditions to SEQ ID NO:10 or the complement thereof; and

[a nucleic acid sequence encoding] encodes a protein at least about 80% identical to SEQ ID NO:11[; and

a nucleic acid sequence encoding a protein that is immunoreactive with an antibody prepared using SEQ ID NO:11 as an antigen, the antibody being immunoreactive with SEQ ID NO:11] and that has polyhydroxyalkanoate synthase activity;

c) a 3' transcription terminator; and

d) a 3' polyadenylation signal sequence that directs the addition of polyadenylate nucleotides to the 3' end of RNA transcribed from the structural nucleic acid sequence.

14. (Amended) A genetically transformed plant comprising in the 5' to 3' direction:

a) a promoter that directs transcription of a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein;

b) a structural nucleic acid sequence encoding a polyhydroxyalkanoate synthase protein; wherein the structural nucleic acid sequence is [selected from the group consisting of:]

a nucleic acid sequence at least about 80% identical to SEQ ID NO:10[;] that

[a nucleic acid sequence that] hybridizes under stringent conditions to SEQ ID NO:10 or the complement thereof; and

[a nucleic acid sequence encoding] encodes a protein at least about 80% identical to SEQ ID NO:11[; and

a nucleic acid sequence encoding a protein that is immunoreactive with an antibody prepared using SEQ ID NO:11 as an antigen, the antibody being immunoreactive with SEQ ID NO:11]; and that has polyhydroxyalkanoate synthase activity;

c) a 3' transcription terminator; and

d) a 3' polyadenylation signal sequence that directs the addition of polyadenylate nucleotides to the 3' end of RNA transcribed from the structural nucleic acid sequence.

Please add new claims 24 and 25.

24. The nucleic acid segment, vector, or cell of claims 1, 2, 4, 5, or 6, wherein the nucleic acid sequence is SEQ ID NO:8.

25. The nucleic acid segment, vector or cell of claims 9, 11, 12, 13, or 14 wherein the nucleic acid sequence is SEQ ID NO:10.

Remarks

Claims 1, 3-6, 9, and 11-14 are pending. The claims have been amended as discussed below to clarify and limit the claimed subject matter. Claims 3-6 and 11-14 have also been amended to clarify the grammar. New claims 24 and 25 are specific to the disclosed sequences. These claims should be entered since they do not introduce new matter and materially reduce the issues on appeal since the examiner has stated that only claims limited to the disclosed sequences are patentable under 35 U.S.C. 112.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1, 3-6, 9, and 11-14 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The claims have been amended to require a defined degree of sequence identify to specific nucleotide sequences, hybridization to the specific nucleotide sequence under stringent conditions, and encoding a protein with a defined enzymatic activity. The substrate specificity of the reductase is demonstrated by Table 6 on page 61 (crotonyl CoA is 4 carbon chain). With the exception of the substrate specifity, the claim elements were individually, in the alternative, the elements of the claims prior to amendment; the amendment makes all elements required.

A description as filed is presumed to be adequate, unless and until the examiner establishes a *prime facie* case by providing reasons why a person skilled in the art at the time the

application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed. (See, e.g., *In re Marzocchi*, 439 F. 2d 220, 224, 169 USPQ 367, 370 (CCPA 1971), MPEP §2163.04).

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. (See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406). A "representative number of species" means that the species which are adequately described are representative of the entire genus. There may be situations where even one species can adequately supports a genus (see, e.g., *Rasmussen*, 650 F.2d at 1214, 211 USPQ at 326-27; In re *Herschler*, 591 F.2d at 1214, 211 USPQ at 326-27). When there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. (See, e.g., MPEP §2163)

The claimed genus require common elements or attributes of the sequences, i.e., there be a nucleic acid sequence which is at least about 80% identical to SEQ ID NO: 8 encoding a 3-ketoacyl-CoA reductase protein or at least about 80% identical to SEQ ID NO: 10 encoding a polyhydroxyalkanoate synthase protein. (See claims 1, 3-6, 9, and 11-14, as amended). One of skill in the art would be able to describe and identify sequences which meet such a structural limitations requirements, i.e., determine the species of the claimed genus, without undue experimentation, based on the written description in the specification.

The discussion regarding introns and splice variants appears to be misplaced since the claimed subject matter relates to bacterial DNA and sequence. It is very unlikely that bacterial

DNA coding sequences contain introns. See, e.g., J. Bacteriol.,182(19):5281-5289 (October 2000). Similarly, it is also very unlikely for bacteria to have splice variants.

A person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the limitation of "at least about 80%" homology to SEQ ID NO: 8 or SEQ ID NO: 10 set forth in the claims yield structurally similar DNAs. Thus, a representative number of species is disclosed, since the homology limitation in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that Applicants were in possession of the claimed subject matter. The claimed subject matter is therefore adequately described. (See Example 9 in p. 35-37 of USPTO's Revised Interim Writing Description Guidelines Training Materials).

In the office action, the Examiner alleged that "[t]he species specifically disclosed are not representative of the genus because the genus is highly variant", but failed to provide evidence that within the genus, there is substantial variation, which the species described cannot reflect. Hence, the Examiner did not establish a *prime facie* case by providing reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed.

The Examiner cited *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993), *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016, *Fiddes v. Baird* 30 USPQ2d 1481, 1483, and *University of California v. Eli Lili & Co.* 43 USPQ 2d 1398, 1404, 1405. Based on the cases, the Examiner alleged that the nucleic acid itself is required. This requirement should not be applicable to the present application, since the requirement is only applicable in certain

situations that are vastly distinct from that of the present application. Under *Fiers v. Revel*, an application does not meet the description requirement as to an invention defined as DNA encoding for a human protein even though it discloses a method for obtaining that DNA. Under *University of California v. Eli Lili & Co*, a cDNA is not defined or described by the mere name "cDNA", even if accompanied by the name of the protein that it encodes. In other words, a DNA sequence cannot be defined the protein encoded by the DNA. In the present application, as discussed above, both DNA sequence and protein sequence are disclosed for certain species within the claimed genus.

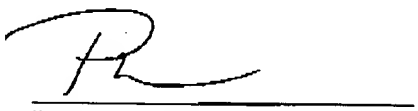
Under *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, the human EPO gene could not have been identified and isolated with a reasonable likelihood of success where neither its DNA nucleotide sequence nor its exact degree of homology with the monkey EPO gene wan known at the time. Under *Fiddes v. Baird*, which cited the *Amgen* case, the genus of mammalian FGF cannot be defined by the species of bovine FGF sequence. In the present case, the claimed genus is defined by known DNA/protein sequences and 80% homology to the known sequences (SEQ ID Nos: 8-11). A sequence with less than 80% homology to SEQ ID Nos: 8-11 does not belong to the genus, even it is from the group of corresponding sequences, mutated sequences, allelic variants, and splice variants.

The Examiner also cited *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111. Under *Vas-Cath Inc. v. Mahurkar*, applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she is in possession of the invention. As discussed above, it is

clear to one skilled in the art that the Applicants is in possession of the claimed subject matter, as of the filing date.

Allowance of claims 1, 3-6, 9, and 11-14, as amended, is earnestly solicited.

Respectfully submitted,



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Date: February 25, 2002

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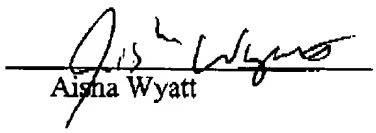
CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this Amendment and Response to Office Action , along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Commissioner for Patents, Washington, D.C. 20231.



Aisha Wyatt

Date: February 25, 2002